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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/086,748	02/28/2002	Paul K. Wolber	10020405-1	8764

7590 06/30/2005

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EXAMINER	
ZHOU, SHUBO	

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 06/30/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/086,748	WOLBER ET AL.	
	Examiner	Art Unit	
	Shubo (Joe) Zhou	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 November 2004 and 03 March 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8 and 10-12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8 and 10-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *11 June 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicants' amendments and request for reconsideration in the communication filed on 11/5/04 and 3/3/05 are acknowledged and the amendments entered.

The objection to the specification set forth in the previous Office action mailed 6/30/04 is hereby withdrawn in view of applicants' amendments to the specification.

The rejection of claims 1-9 under 35 U.S.C. 112 , second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention set forth in the previous Office action mailed 6/30/04 is hereby withdrawn in view of applicants' amendment to claim 1.

The compact discs containing the sequence listing under 37 CFR 1.821(c) and the computer readable form of the listing under 37 CFR 1.821(e) as well as a statement under 37 CFR 1.821(f) filed on 3/3/05 are received. The computer readable form has not yet been entered as the evaluation thereof has not been completed.

Claim Rejections-35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, and 7-8 are rejected under 35 U.S.C. 102(b) as being anticipated by Lockhart et al. (IDS document: WO 97/10365, 3/20/1997).

The claims are drawn to a method of calibrating molecular array data comprising using a molecular array containing calibrating probes that hybridize to a sufficient fraction of target molecules in a sample to produce a signal intensity, and normalizing signals of features on the array using the calibrating probes by calculating a collective signal intensity. Due to lack of a specific definition for the term "collective signal intensity" in the specification, it is interpreted as total signal intensities of the calibrating probes (collective: assembled or accumulated into a whole. Dictionary.com http://dictionary.reference.com/search?q=collective).

Lockhart et al. disclose a method of using oligonucleotide array for monitoring gene expression. The method comprises using an array containing not only oligonucleotide probes referred to as "test probes", but also control probes used for calibration. The control probes include normalization controls, expression level controls such as probes from housekeeping genes, and mismatch controls. In one embodiment, Lockhart et al. teach that the difference between signal intensities of a perfect match (PM) probe and a mismatch (MM) probe for each pair of PM and MM are calculated, and then the average of the differences for all the pairs is calculated. See page 61, first paragraph and page 103, claims 66-67. It would be readily recognized by one of skill in the art that when the average difference is calculated, a total intensity of the difference between the PM and MM must have also been calculated. Consequently, the total intensities of all MM probes are also calculated. All the control probes disclosed by Lockhart et al. are interpreted as calibrating probes as in the instant claims because they are used to calibrate the signals of the test probes. The calibrating probes disclosed by

Lockhart et al. will hybridize to a fraction of the target molecules in the sample solutions to which the array is exposed for hybridization because the products of the housekeeping genes, etc. are contained in the sample solutions. Further, since MM probes for each target is included as a control probes, which will hybridize to its target under certain stringencies albeit maybe nonspecifically. Since the specification does not explicitly define the term "sufficient fraction of target molecules", it is broadly interpreted as any fraction that is sufficient to generate a signal by either specific or nonspecific hybridizations.

In regard to claims 7-8, which require that a set of similar calibrating signal intensities that each covers a discrete range of signal intensities generated from the features of the array, Lockhart et al. teach that each PM signal intensity is calibrated by calculating the difference between signal intensities of the PM and its corresponding MM. The signal intensity for every PM probe is similarly calibrated. The average difference for all PM/MM is also calculated. Each signal can then be calibrated thereupon. Each of these PM-MM signal intensities is interpreted as a calibrating signal intensity. Since all the differences of PM-MM are calculated similarly, they are interpreted as similar calibrating signal intensities. Because these differences of PM-MM as a whole represents the signal intensities for all the probes on the array, they cover the entire span, i.e. overall range of signal intensities generated from the array.

probe for each pair of PM and MM are calculated, and then the average of the differences for all the pairs is calculated. See page 61, first paragraph and page 103, claims 66-67.

Claim Rejections-35 USC § 103

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

16. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

17. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

18. Claims 1-3, 5, and 7-8, and 10-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lockhart et al. (WO 97/10365, 3/20/1997), as applied to claims 1, and 7-9

above, in view of Chenchik et al. (US patent no. 6,077,673, Date of Patent: June 20, 2000) and further in view of Lewin, B., (Genes IV, 1990, Oxford University Press).

The instant claims are drawn to a method of calibrating molecular array data comprising using a molecular array containing calibrating probes that either hybridize to a sufficient fraction of target molecules in a sample solution to which the array is exposed for hybridization or hybridize to a majority of target molecules in the sample solution, and normalizing signals of features on the array using the calibrating probes by calculating a collective signal intensity. Claims 2-3 also require that the calibrating probes are poly(A) oligonucleotides.

As applied to claims 1, and 7-9, above, Lockhart et al. disclose a method of using oligonucleotide array for monitoring gene expression. The method comprises using an array containing not only oligonucleotide probes referred to as "test probes", but also control probes used for calibration. The control probes include normalization controls, expression level controls such as probes from housekeeping genes, and mismatch controls. In one embodiment, Lockhart et al. teach that the difference between signal intensities of a perfect match (PM) probe and a mismatch (MM) probe for each pair of PM and MM are calculated, and then the average of the differences for all the pairs is calculated. See page 61, first paragraph and page 103, claims 66-67. It would be readily recognized by one of skill in the art that when the average difference is calculated, a total intensity of the difference between the PM and MM must have also been calculated. Consequently, the total intensities of all MM probes are also calculated. All the control probes disclosed by Lockhart et al. are interpreted as calibrating probes as in the instant claims because they are used to calibrate the signals of the test probes. The calibrating probes disclosed by Lockhart et al. will hybridize to a fraction of the target molecules in the sample

solutions to which the array is exposed for hybridization because the products of the housekeeping genes, etc. are contained in the sample solutions. Further, since MM probes for each target is included as a control probes, which will hybridize to its target under certain stringencies albeit maybe nonspecifically. Since the specification does not explicitly define the term "sufficient fraction of target molecules", it is broadly interpreted as any fraction that is sufficient to generate a signal by either specific or nonspecific hybridizations.

However, Lockhart et al. do not explicitly recite that poly(A) oligonucleotides are used as calibrating probes, and that the calibrating probes hybridize to a majority of the target molecules in the sample solution to which the array is exposed.

Chenchik et al. disclose a nucleic acid microarray and a process of using same for gene expression monitoring. The array is exposed to a sample solution containing cDNA molecules derived from the mRNA from a biological sample. In addition to the "probe spots", the array also comprises "calibration spots" and "control spots" (column 4, lines 12-20). Chenchik et al. indicate that the calibrating and control spots are to "provide other useful information, such as background or basal level of expression, and the like', and such spots "serve in the normalization of mRNA abundance and standardization of hybridization signal intensity in the sample assayed with the array" (column 8, lines 50-67 and column 9). While Chenchik et al. do not explicitly disclose using poly(A) oligonucleotides as calibrating spots, they do motivate/suggest doing such by emphasizing that the calibrating probes should not be unique to a particular target in the sample, but "common" to the targets (column 8, lines 50-67).

A person of ordinary skill in the art would have been motivated by Chenchik et al. to search for probes that are common to the targets in the sample solution to modify Lockhart et al. to provide more calibrating probes for the microarray analysis.

Lewin teaches that poly(A) tail is common to eukaryotic, such as human mRNA. See pages 178-179. Since the target molecules contained in the sample solutions to which the array is exposed for hybridization in the method disclosed by Lockhart et al. are cDNAs, and since the cDNAs are derived from mRNAs by reverse transcription using oligo(dT) as primers followed by PCR amplification (Lockhart et al. page 39), it would have been obvious to one of ordinary skill in the art that oligo(dT) or poly(A) would be commonly present in the cDNA targets due to the way they are made, and one of ordinary skill in the art would have been motivated by Lewin and Chenchik et al. to modify the method of Lockhart et al. to include poly(A) oligonucleotides on the array as extra calibrating probes. Such poly(A) oligonucleotides would hybridize to the majority of the target molecules due to the presence of poly(T) thereon. There would have been a reasonable expectation of success because Lockhart et al. and Chenchik et al. provide the details of procedures for making an array, preparing cDNA samples for hybridization, and making poly(A) oligonucleotides would have been known and routine skill in the art. Note that by poly(A) oligonucleotides it is meant that the oligonucleotides consist of, or comprise, consecutive multiple "As".

Such poly(A) oligonucleotides calibrating probes would be complementary to oligo(dT) which is a synthetic nucleotide sequence that is appended to primers for reverse transcription of the mRNA molecules during the process of preparing target molecules for hybridization. This thus reads on the specific requirement by claim 5.

19. Claims 1, 4, and 7-8, and 10-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lockhart et al. (WO 97/10365, 3/20/1997), as applied to claims 1, and 7-9 above, in view of Chenchik et al. (US patent no. 6,077,673, Date of Patent: June 20, 2000) and further in view of Darnell et al. (Molecular Cell Biology, Eds., 1990, published by Scientific American Books).

The instant claims are drawn to a method of calibrating molecular array data comprising using a molecular array containing calibrating probes that either hybridize to a sufficient fraction of target molecules in a sample solution to which the array is exposed for hybridization or hybridize to a majority of target molecules in the sample solution, and normalizing signals of features on the array using the calibrating probes by calculating a collective signal intensity. Claim 4 also requires that the calibrating probes comprise Alu repeat sequences.

As applied to claims 1, and 7-9, above, Lockhart et al. disclose a method of using oligonucleotide array for monitoring gene expression. The method comprises using an array containing not only oligonucleotide probes referred to as "test probes", but also control probes used for calibration. The control probes include normalization controls, expression level controls such as probes from housekeeping genes, and mismatch controls. In one embodiment, Lockhart et al. teach that the difference between signal intensities of a perfect match (PM) probe and a mismatch (MM) probe for each pair of PM and MM are calculated, and then the average of the differences for all the pairs is calculated. See page 61, first paragraph and page 103, claims 66-67. It would be readily recognized by one of skill in the art that when the average difference is calculated, a total intensity of the difference between the PM and MM must have also been

calculated. Consequently, the total intensities of all MM probes are also calculated. All the control probes disclosed by Lockhart et al. are interpreted as calibrating probes as in the instant claims because they are used to calibrate the signals of the test probes. The calibrating probes disclosed by Lockhart et al. will hybridize to a fraction of the target molecules in the sample solutions to which the array is exposed for hybridization because the products of the housekeeping genes, etc. are contained in the sample solutions. Further, since MM probes for each target is included as a control probes, which will hybridize to its target under certain stringencies albeit maybe nonspecifically. Since the specification does not explicitly define the term "sufficient fraction of target molecules", it is broadly interpreted as any fraction that is sufficient to generate a signal by either specific or nonspecific hybridizations.

However, Lockhart et al. do not explicitly recite that oligonucleotide comprising Alu sequences are used as calibrating probes, and that the calibrating probes hybridize to a majority of the target molecules in the sample solution to which the array is exposed.

Chenchik et al. disclose a nucleic acid microarray and a process of using same for gene expression monitoring. The array is exposed to a sample solution containing cDNA molecules derived from the mRNA from a biological sample. In addition to the "probe spots", the array also comprises "calibration spots" and "control spots" (column 4, lines 12-20). Chenchik et al. indicate that the calibrating and control spots are to "provide other useful information, such as background or basal level of expression, and the like', and such spots "serve in the normalization of mRNA abundance and standardization of hybridization signal intensity in the sample assayed with the array" (column 8, lines 50-67 and column 9). While Chenchik et al. do not explicitly disclose using Alu oligonucleotides as calibrating spots, they do motivate/suggest doing such by

emphasizing that the calibrating probes should not be unique to a particular target in the sample, but "common" to the targets (column 8, lines 50-67).

A person of ordinary skill in the art would have been motivated by Chenchik et al. to search for probes that are common to the targets in the sample solution to modify Lockhart et al. to provide more calibrating probes for the microarray analysis.

Darnell et al. teach that Alu sequence is common to human genes and mRNA (see pages 373-374). It would have been obvious to one of ordinary skill in the art that such common Alu sequence would meet the requirement for a calibrating probe set by Chenchik et al. Thus, one of ordinary skill in the art would have been motivated by Chenchik et al. and Darnell et al. to modify the method of Lockhart et al. to include oligonucleotides comprising Alu sequences on the array as extra calibrating probes. There would have been a reasonable expectation of success because Lockhart et al. and Chenchik et al. provide the details of procedures for making an array, preparing cDNA samples for hybridization, and making oligonucleotides comprising Alu sequence would have been known and routine skill in the art.

Therefore, the invention would have been obvious to a person of ordinary skill in the art at the time the invention was made.

20. Claims 1, 6-8, and 10-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lockhart et al. (WO 97/10365, 3/20/1997), as applied to claims 1, and 7-9 above, in view of Chenchik et al. (US patent no. 6,077,673, Date of Patent: June 20, 2000) and further in view of Feinberg et al. (Analytical Biochemistry, Vol. 132, pages 6-13, 1983).

The instant claims are drawn to a method of calibrating molecular array data comprising using a molecular array containing calibrating probes that either hybridize to a sufficient fraction of target molecules in a sample solution to which the array is exposed for hybridization (as required in claims 1-9), or hybridize to a majority of target molecules in the sample solution (as required in claims 10-14), and normalizing signals of features on the array using the calibrating probes by calculating a collective signal intensity. Claim 6 also requires that the calibrating probes are random sequence oligonucleotide.

As applied to claims 1, and 7-9, above, Lockhart et al. disclose a method of using oligonucleotide array for monitoring gene expression. The method comprises using an array containing not only oligonucleotide probes referred to as "test probes", but also control probes used for calibration. The control probes include normalization controls, expression level controls such as probes from housekeeping genes, and mismatch controls. In one embodiment, Lockhart et al. teach that the difference between signal intensities of a perfect match (PM) probe and a mismatch (MM) probe for each pair of PM and MM are calculated, and then the average of the differences for all the pairs is calculated. See page 61, first paragraph and page 103, claims 66-67. It would be readily recognized by one of skill in the art that when the average difference is calculated, a total intensity of the difference between the PM and MM must have also been calculated. Consequently, the total intensities of all MM probes are also calculated. All the control probes disclosed by Lockhart et al. are interpreted as calibrating probes as in the instant claims because they are used to calibrate the signals of the test probes. The calibrating probes disclosed by Lockhart et al. will hybridize to a fraction of the target molecules in the sample solutions to which the array is exposed for hybridization because the products of the

housekeeping genes, etc. are contained in the sample solutions. Further, since MM probes for each target is included as a control probes, which will hybridize to its target under certain stringencies albeit maybe nonspecifically. Since the specification does not explicitly define the term "sufficient fraction of target molecules", it is broadly interpreted as any fraction that is sufficient to generate a signal by either specific or nonspecific hybridizations.

However, Lockhart et al. do not explicitly recite that random sequence oligonucleotide are used as calibrating probes, and that the calibrating probes hybridize to a majority of the target molecules in the sample solution to which the array is exposed.

Chenchik et al. disclose a nucleic acid microarray and a process of using same for gene expression monitoring. The array is exposed to a sample solution containing cDNA molecules derived from the mRNA from a biological sample. In addition to the "probe spots", the array also comprises "calibration spots" and "control spots" (column 4, lines 12-20). Chenchik et al. indicate that the calibrating and control spots are to "provide other useful information, such as background or basal level of expression, and the like', and such spots "serve in the normalization of mRNA abundance and standardization of hybridization signal intensity in the sample assayed with the array" (column 8, lines 50-67 and column 9). While Chenchik et al. do not explicitly disclose using random sequence oligonucleotides as calibrating spots, they do motivate/suggest doing such by emphasizing that the calibrating probes should not be unique to a particular target in the sample, but "common" to the targets (column 8, lines 50-67).

A person of ordinary skill in the art would have been motivated by Chenchik et al. to search for probes that are common to the targets in the sample solution to modify Lockhart et al. to provide more calibrating probes for the microarray analysis.

Feinberg et al. teach a method of labeling a DNA by using a mixture of random hexamer as primers and state that the oligonucleotides bind to any DNA in high frequency. see page 6, abstract and pages 7-11). It would have been obvious to one of ordinary skill in the art that the random hexamer oligonucleotides would be ideal for a calibrating probe because it would meet the "common" standard proposed by Chenchik et al. One of ordinary skill in the art would have been motivated by Feinberg et al. and Chenchik et al. to modify the method of Lockhart et al. to include random hexamer oligonucleotides on the array as extra calibrating probes. There would have been a reasonable expectation of success because Lockhart et al. and Chenchik et al. provide the details of procedures for making an array, preparing cDNA samples for hybridization, and making random hexamer oligonucleotides would have been known and routine skill in the art, and the random primers would have been actually commercially available.

Therefore, the invention would have been obvious to a person of ordinary skill in the art at the time the invention was made.

Response to Arguments

Applicants did not separately argue to each rejection, but rather argued altogether focusing on the reference of Lockhart et al.

Applicants' arguments filed 11/5/04 have been fully considered but they are not persuasive for the following reasons:

Applicants first argue that the reference of Lockhart et al., as well as other references, does not disclose one requirement in claim 1, i.e. the array "containing calibrating probes that hybridize to a sufficient fraction of target molecules in sample solutions." Applicants argue that

none of the control probes, including the mismatch probes, normalization probes and expression level controls, will hybridize to a sufficient fraction of target molecules. See pages 9-15 of the communication filed 11/5/04. This is not considered persuasive. Let's take the mismatch (MM) controls as an example. Lockhart et al. disclose that the array contain a MM probe for each PM probe, and the hybridization signals are evaluated by calculating the difference between signal intensities of the PM probe and the MM probe for each pair and the average of the differences for all the pairs. The reason to have these MM probes on the array in the first place and to calculate the differences between PM and MM after hybridization is that the MM probes will hybridize to their corresponding target molecules or other target molecules at certain stringencies through either specific or nonspecific hybridizations. It should be pointed out that claim 1 merely recites the array "containing calibrating probes that hybridize to a sufficient fraction of target molecules in sample solutions" without explicitly setting forth the hybridization conditions or the nature of hybridizations, i.e. specific versus nonspecific. Further, since the specification does not explicitly define the term "sufficient fraction of target molecules", it is broadly interpreted as any fraction that is sufficient to generate a signal by either specific or nonspecific hybridizations.

Applicants further argue that Lockhart et al. and other references do not disclose what is required by the dependent claim 7, i.e. generating a set of similar calibrating signal intensities that cover all the discrete ranges of the overall signal intensities generated from the array. This is not deemed persuasive because Lockhart et al. teach that each PM signal intensity is calibrated by calculating the difference between signal intensities of the PM and its corresponding MM. The signal intensity for every PM probe is similarly calibrated. The average difference for all PM/MM is also calculated. Each signal can then be calibrated thereupon. Each of these PM-MM

signal intensities is interpreted as a calibrating signal intensity. Since all the differences of PM-MM are calculated similarly, they are interpreted as similar calibrating signal intensities. Because these differences of PM-MM as a whole represents the signal intensities for all the probes on the array, they cover the entire span, i.e. all the discrete ranges of signal intensities generated from the array.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL.

Applicants are reminded of the extension of time policy as set forth in 37 C.F.R. §1.136 (a). A shortened statutory period for response to this final action is set to expire three months from the date of this action. In the event a first response is filed within two months of the mailing date of this final action and the advisory action is not mailed until after the end of the three-month shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. §1.136 (a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than six months from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shubo (Joe) Zhou, whose telephone number is 571-272-0724.

The examiner can normally be reached Monday-Friday from 8 A.M. to 4 P.M. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, Ph.D., can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Patent Analyst Tina Plunkett whose phone number is (571) 272-0549.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Shubo (Joe) Zhou, Ph.D.

Patent Examiner

23 June 2005

JOHN S. BRUSCA, PH.D
PRIMARY EXAMINER